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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/554,076	05/29/2007	Stephen H. Leppla	015280-478100US	4475
45115 7590 12/24/2008 TOWNSEND AND TOWNSEND AND CREW, LLP TWO EMBARCADERO CENTER 8TH FLOOR SAN FRANCISCO, CA 94111				
EXAMINER				
CANELLA, KAREN A				
ART UNIT		PAPER NUMBER		
1643				
MAIL DATE		DELIVERY MODE		
12/24/2008		PAPER		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/554,076

Applicant(s)

LEPPLA ET AL.

Examiner

Karen A. Canella

Art Unit

1643

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-49 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-49 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SF 298)
Paper No(s)/Mail Date ____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date ____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: ____

DETAILED ACTION

Claim 5 has been amended. Claims 1-49 are pending and under consideration.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 41, 46 and 47 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 41 is vague and indefinite in the recitation of "also overexpressed" in reference to claim 40. Claim 40 does not state that any protein need be overexpressed. amendment of the claim to delete the word "also" would overcome this rejection.

The recitation of "the cancer cell" in claims 46 and 47 lacks specific antecedent basis in claim 40.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 24-29, 31-39 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating cancer comprising the administration of a DT fusion toxin comprising a heterologous polypeptide which specifically binds to a protein overexpressed on the surface of a cancer cell, does not reasonably provide enablement for a method of treating cancer comprising the administration of a DT fusion toxin comprising a heterologous polypeptide which specifically binds to a protein overexpressed on the surface of a cancer cell. The specification does not enable any person skilled in the art to which it pertains,

or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. In re wands, 858 F.2d 731, 737.8 USPQ2d 1400, 1404 (Fed. Cir. 1988)..

Claims 24-29, 31-39 are broadly drawn to encompass the administration of a DT fusion protein comprising a heterologous polypeptide, wherein the heterologous polypeptide binds to the surface of a generic "cell". The method objective of claim 24 is the treatment of cancer, Claim 30 which is a non-rejected dependent claim requires that said cell be a cancer cell. Thus, when given the broadest reasonable interpretation, claims 24-29 and 31-39 encompass the targeting of cells which are not cancer cells via overexpressed receptors. The art at the time of filing teaches the structural identity of overexpressed receptors on cancer cells. The specification fails to teach the structural identity of over expressed surface receptors on non-cancerous cells which would provide for a method of treating cancer by targeting said non-cancerous receptor via the heterologous portion of the DT fusion protein. The scope of the claims must be commensurate with the scope of the enablement set forth. without further teachings in the specification, one of skill in the art must first identify receptors on non-cancerous cells which would provide for a method of treating cancer, and therefore one of skill in the art would be subject to undue experimentation in order to practice the broadly claimed method of treating cancer.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 49 is rejected under 35 U.S.C. 102(b) as being anticipated by Benatti et al (WO 96/01893, January 1996).

Claim 49 is drawn in part to an isolated nucleic acid comprising SEQ ID NO:14.

Benatti et al disclose Sequence Identifier 12 (page 22, line 25) which is identical to the instant SEQ ID NO:14.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-6, 8, 11, 12, 17, 20-22, 24-30, 32, 34, 35, 40-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Leppla et al (WO 01/21656) in view of Leppla et al (U.S. 5,677,274) and Frankel et al ('Peptide Toxins Directed at the Matrix Dissolution Systems of Cancer Cells', In: Protein and Peptide Letters, 2002, vol. 9, pp. 1-14).

Claim 1 is drawn to a nucleic acid comprising residues 1-388 of DT, wherein the native furin cleavage site has been substituted for a cleavage site of a matrix metalloproteinase or a plasminogen activator and, a heterologous polypeptide, wherein the heterologous polypeptide specifically binds to a protein overexpressed on the surface of a cell. Claim 2 embodies the

nucleic acid of claim 1 wherein the matrix metalloproteinase is selected from the group consisting of MMP-2 (gelatinase A), MMP-9 (gelatinase B) and membrane type 1 MMP (MT1-MMP). Claim 3 embodies the nucleic acid of claim 1, wherein the plasminogen activator is selected from the group consisting of tissue plasminogen activator (t-PA) and urokinase plasminogen activator (u-PA). Claim 4 embodies the nucleic acid of claim 1 wherein the metric metalloproteinase cleavage sites are GPLGMLSQ and GPLGLWAQ. Claim 5 embodies the nucleic acid of claim 1 wherein the plasminogen activator site is selected from the group consisting of QRGRSA, GSGRSA and GSGKSA. Claim 6 embodies the nucleic acid of claim 1, wherein the protein overexpressed on the surface of a cell is a receptor. Claim 12 embodies the nucleic acid of claim 6 wherein the cell is a cancer cell. Claim 12 embodies the nucleic acid of claim 12 wherein the cancer is leukemia. Claim 22 specifies that the leukemia is AML. Claim 8 embodies the nucleic acid of claim 1 wherein the heterologous polypeptide comprises a growth factor.

Claim 11 is drawn to a vector comprising the nucleic acid of claim 1. Claim 20 is drawn to a host cell comprising the vector of claim 11.

Claim 17 is drawn to a polypeptide encoded by the nucleic acid of claim 1.

Claim 24 is drawn to a method of treating cancer comprising administering to a subject a DT fusion protein comprising residues 1-388 of DT, wherein the native furin cleavage site has been substituted for a cleavage site for a matrix metalloproteinase or a plasminogen activator and a heterologous polypeptide which specifically binds to a protein overexpressed of the surface of a cell. Claim 25 embodies the method of claim 24 wherein the matrix metalloproteinase is selected from the group consisting of MMP-2 (gelatinase A), MMP-9 (gelatinase B) and membrane type 1 MMP (MT1-MMP). Claim 26 embodies the method of claim 24, wherein the plasminogen activator is selected from the group consisting of tissue plasminogen activator (t-PA) and urokinase plasminogen activator (u-PA). Claim 27 embodies the method of claim 24 wherein the metric metalloproteinase cleavage sites are GPLGMLSQ and GPLGLWAQ. Claim 28 embodies the method of claim 24 wherein the plasminogen activator site is selected from the group consisting of QRGRSA, GSGRSA and GSGKSA. Claim 29 embodies the method of claim 24, wherein the protein overexpressed on the surface of a cell is a receptor. Claim 30 embodies the method of claim 24 wherein the cell is a cancer cell. Claim 34 embodies the

method of claim 30, wherein the cancer is leukemia. Claim 25 specifies that the leukemia is AML. Claim 32 embodies the method of claim 24 wherein the heterologous polypeptide comprises a growth factor.

Claim 40 is drawn in part to a method of targeting a compound to a cell overexpressing a growth factor receptor comprising administering to the cells a DT fusion protein comprising residues 1-388 of DT, wherein the native furin cleavage site has been substituted for a cleavage site for a matrix metalloproteinase or a plasminogen activator and a heterologous polypeptide which specifically binds to a growth factor receptor. Claim 41 embodies the method of claim 40 wherein the cell expresses matrix metalloproteinase, a t-PA or a u-PA. Claim 42 embodies the method of claim 40 wherein the matrix metalloproteinase is selected from the group consisting of MMP-2 (gelatinase A), MMP-9 (gelatinase B) and membrane type 1 MMP (MT1-MMP). Claim 43 embodies the method of claim 40, wherein the plasminogen activator is selected from the group consisting of tissue plasminogen activator (t-PA) and urokinase plasminogen activator (u-PA). Claim 44 embodies the method of claim 40 wherein the matrix metalloproteinase cleavage sites are GPLGMLSQ and GPLGLWAQ. Claim 45 embodies the method of claim 40 wherein the plasminogen activator site is selected from the group consisting of QRGRSA, GSGRSA and GSGKSA. Claim 46 embodies the method of claim 40, wherein the cell is leukemia cell. Claim 47 specifies that the leukemia cell is an AML cell.

Leppla et al (WO01/21656) teaches a method of targeting a cell overexpressing matrix metalloproteinase or plasminogen activator, wherein said cells include cancer cells such as leukemia and myelogenous leukemia, comprising administering to said cells a recombinant anthrax protein wherein said protein comprises matrix metalloproteinase cleavage sites, plasminogen activator cleavage sites in place of the native furin-recognized cleavage site (page 6, line 1 to page 7, line 8 and page 7, lines 23-27, page 13, lines 23-26). Leppla et al teach a specific embodiment wherein said recombinant protein comprises a heterologous receptor binding domain which is a growth factor (page 7, lines 19-22). Leppla et al teach that the recombinant proteins kill tumor cells without serious damage to normal cells (page 13, lines 29-33).

Leppla et al ('274) teach that any specific protease site can be introduced into any natural or recombinant toxin, including diphtheria toxin, for which proteolytic cleavage is required (column 10, lines 28-51).

Frankel et al teach that DT comprises an N-terminal catalytic domain, a furin-sensitive loop and a translocation domain (amino acids 1-388) followed by a cell-binding domain (amino acids 389-535) (page 8, lines 1-6). Frankel et al teach that the cell binding domain of DT binds to heparin-binding epidermal growth factor-like growth factor undergoes internalization via clathrin-coated pits and furin cleavage and the catalytic domain is then transferred into the cytosol resulting in ADP-ribosylation of elongation factor-2 and inactivation of protein synthesis and cell death (page 8, lines 6-12). One of skill in the art would reasonably ascertain that the cell binding domain of native DT did not exert cell-type specificity because heparin-binding epidermal growth factor does not exhibit cell type specificity. Frankel et al teach the fusion of the catalytic and translocation domains of DT without the cell binding domain of DT fused to u-PA, but notes the damage to human endothelial cells in vitro. It is noted that the fusion protein described by Frankel et al retained the native furin cleavage site.

It would have been *prima facie* obvious at the time that the claimed invention was made to substitute residues 1-388 of DT, wherein said DT had been recombinantly engineered in a similar manner as the anthrax toxin to replace the furin cleavage site with matrix metalloproteinase cleavage sites, or plasminogen activator cleavage sites, wherein the recombinant DT was also a fusion protein with a growth factor, for binding to cells which overexpress said growth factor. One of skill in the art would have been motivated to do so by the teachings of Leppla et al ('274) on the substitution of any specific protease site within a natural or recombinant toxin, such as DT, and the teachings of Frankel et al on the catalytic and translocation domains of DT in addition to the location of the furin cleavage sites. One of skill in the art would have been motivated to leave out the cell binding domain of DT (residues 389-535) because said cell binding domain would lead to non-specific binding and substitute the growth factor in order to target cell or cancer cells which overexpress growth factor receptors.

Claims 1-13, 16-36, 39-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Leppla et al (WO 01/21656), Leppla et al (U.S. 5,677,274) and Frankel et al ('Peptide Toxins

Directed at the Matrix Dissolution Systems of Cancer Cells', In: Protein and Peptide Letters, 2002, vol. 9, pp. 1-14), as applied to claims 1-6, 8, 11, 12, 17, 20-22, 24-30, 32, 34, 35, 40-47 above, and further in view of Frankel et al (Clinical Cancer Research, May 2002, Vol. 8, pp. 1004-1013) and Scherrer et al (British Journal of Haematology, 1999, Vol. 105, pp. 920-927).

Claim 7 embodies the nucleic acid of claim 1 wherein the heterologous protein comprises a cytokine. Claim 13 specifies that the heterologous polypeptide comprises GM-CSF. Claim 9 embodies the nucleic acid of claim 1 wherein the heterologous protein is selected from a group including GM-CSF. Claim 10 embodies the method of claim 1 wherein the nucleotide sequence is elected from SEQ ID NO:2-13. Claim 18 embodies the polypeptide encoded by the nucleic acid of claim 10, SEQ ID NO:2. Claim 23 is drawn to a pharmaceutical composition comprising the protein of claim 18 and a pharmaceutically acceptable carrier

Claim 16 is drawn to a nucleic acid encoding a D fusion protein comprising residues 1-388 of DT wherein the native furin cleavage site has been substituted for a cleavage site for a u-PA and GM-CSF. Claim 19 is drawn to the polypeptide encoded by the nucleic acid of claim 16.

Claim 31 embodies the method of claim 24 wherein the heterologous polypeptide comprises a cytokine. Claim 36 embodies the method of claim 31 wherein the heterologous polypeptide comprises GM-CSF. Claim 33 specifies that the suion protein is encoded by a nucleotide sequence selected from SEQ ID NO:2-13.

Claim 39 is drawn to the method of claim 24 wherein the DT fusion protein comprises residues 1-388 of DT wherein the native furin cleavage site has been substituted for a cleavage site for a u-PA, and GM-CSF.

Claim 40 specifies that the heterologous polypeptide specifically binds to a cytokine receptor. Claim 48 embodies the method of claim 40 wherein the DT fusion protein comprises residues 1-388 of DT wherein the native furin cleavage site has been substituted for a cleavage site for a u-PA and GM-CSF.

Claim 49 is drawn in part to an isolated nucleic acid selected from a group consisting of SEQ ID NO:2-13..

The combination of Leppla et al (WO 01/21656), Leppla et al (U.S. 5,677,274) and Frankel et al render obvious the instant claims to the extent that the engineered DT fusion protein

comprises a growth factor. The combination does not provide for an engineered DT fusion protein which comprises as the heterologous protein, GM-CSF.

Frankel et al (2002) teach the administration of a DT fusion protein wherein the heterologous protein is GM-CSF,. One of skill in the art would reasonable conclude that the DT of Frankel comprised the native furin binding site. Frankel et al teach that the DT fusion protein provided a low level of clinical activity in patients with chemoresistant AML, and that liver toxicity precluded dose escalation. Frankel et al teach that this low level of activity was in contrast to the high level of activity exhibited against cultured cells (page 1012, bridging paragraph between the first and second columns). Frankel et al suggest that liver toxicity was due to the GM-CSF binding Kuffer cells (page (1011, second column, first paragraph).

The abstract of Scherrer et al teaches that leukemic cells from patients with AML exhibited high enzymatic activity for u-PA.

It would have been prima facie obvious to provide the nucleic acid encoding the engineered DT protein rendered obvious by the combination of Leppla et al (WO 01/21656), Leppla et al (U.S. 5,677,274) and Frankel et al wherein the furin cleavage sites were replaced by u-PA cleavage sites and wherein the heterologous protein was GM-CSF. One of skill in the art would have been motivated to do so by the teaching of Frankel et al (2002) on the low level of clinical activity associated with the DT-GM-CSF fusion protein and the potential for liver toxicity, and the teachings of abstract of Scherrer et al on the high level of u-PA enzymatic activity associated with AML cells. One of skill in the art would understand that the use of the u-PA cleavage site in place of the furin cleavage site could further lower the dose of the DT-GM-CSF fusion protein require to treat the chemoresistant AML of Frankel et al because the AML cells overexpress the u-PA enzymatic activity which provides for the cleavage of the cytotoxic domain once internalized by the AML cell via GM-CSF. One of skill in the art would reasonable expect that a lower dose effective to treat AML would result in less liver toxicity due to Kuffer cell binding in the liver.

Claims 1-12, 14, 17, 20-22, 24-35, 37, 40-47 and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Leppla et al (WO 01/21656), Leppla et al (U.S. 5,677,274) and Frankel et al ('Peptide Toxins Directed at the Matrix Dissolution Systems of Cancer Cells', In:

Protein and Peptide Letters, 2002, vol. 9, pp. 1-14), as applied to claims 1-6, 8, 11, 12, 17, 20-22, 24-30, 32, 34, 35, 40-47 above, and further in view of Faller (WO 95/11699, 05-1995).

Claim 9 embodies the nucleic acid of claim 1 wherein the heterologous polypeptide is selected from a group including II-2. Claims 14 embodies the nucleic acid of claim 7, wherein the heterologous protein comprises II-2. Claim 37 embodies the method of claim 31 wherein the heterologous polypeptide comprises II-2. Claim 40 specifies that the heterologous polypeptide specifically binds to a cytokine receptor.

Claim 49 is drawn to an isolated nucleic acid comprising SEQ ID NO:2-18.

Faller et al teach the treatment of leukemia cells with a DAB389-II-2 fusion toxin, wherein DAB389 comprises residues 1-189 of DT.

It would have been prima facie obvious at the time that the claimed invention was made to use II-2 as the heterologous receptor binding protein of the engineered DT-growth factor fusion protein rendered obvious by Leppla et al (WO 01/21656), Leppla et al (U.S. 5,677,274) and Frankel et al. One of skill in the art would have been motivated to do so by the teachings of Faller et al on the treatment of leukemias by administration of the DT-II-2 fusion protein.

Claims 1-6, 8-12, 15, 17, 20-22, 24-30, 32-35, 38, 40-47 and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Leppla et al (WO 01/21656), Leppla et al (U.S. 5,677,274) and Frankel et al ('Peptide Toxins Directed at the Matrix Dissolution Systems of Cancer Cells', In: Protein and Peptide Letters, 2002, vol. 9, pp. 1-14), as applied to claims 1-6, 8, 11, 12, 17, 20-22, 24-30, 32, 34, 35, 40-47 above, and further in view of Heimbrook et al (PNAS, 1990, Vol. 87, pp. 4697-4701).

Claim 9 embodies the nucleic acid of claim 1 wherein the heterologous polypeptide is selected from a group including EGF. Claim 15 embodies the nucleic acid of claim 8 wherein the heterologous polypeptide comprises EGF. Claim 38 embodies the method of claim 32 wherein the heterologous polypeptide comprises EGF.

Heimbrook et al teach fusion proteins with toxins, wherein the heterologous polypeptide is TGF- α which is a ligand for the EGF receptor (page 4697, first paragraph under the abstract). Heimbrook et al teach that many tumors possess EGFR and some tumor types exhibit

increased numbers of EGFR relative to normal tissue making the EGFR an attractive target for delivery of an anticancer agent (page 4697, first column, lines).

It would have been prima facie obvious at the time that the claimed invention was made to provide for an engineered DT fusion protein which comprises as the heterologous protein, EGF for binding to the EGFR. One of skill in the art would have been motivated to do so by the analogous example taught by Heinbrook et al, comprising a ligand which binds to the EGFR and a toxin moiety.

All claims are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A. Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 10-6:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571)272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Karen A Canella/

Primary Examiner, Art Unit 1643

